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Cognitive Behavior Therapy for Fibromyalgia: A Meta-Analysis

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Cognitive Behavior Therapy for Fibromyalgia: A Meta-Analysis

Abstract

Fibromyalgia is a chronic illness involving widespread pain, and many related symptoms such as fatigue, mood disorders, headache, and sleep disturbance. This condition has been traditionally difficult for health care providers to treat with medications. Increasingly, treatment programs for individuals with Fibromyalgia have included psychological therapies such as Cognitive Behavioral Therapy (CBT). CBT has shown preliminary evidence to support its use in Fibromyalgia; however, there is a limited understanding of CBT in this population. This meta-analysis examined all treatment studies, which included at least one group of patients receiving CBT. Functional Status, Pain Symptoms, Depression, Anxiety and Psychological distress were used as separate outcome variables to examine the effects of CBT. A literature review was conducted using Medline, PsycINFO, and the Cochrane Central Register of Controlled Trials. Of the 2000 studies that were found, 29 research studies met criteria for inclusion in the study. This resulted in 1220 participants and 167 effect sizes that could be examined. Effect sizes were corrected using Hedge's correction for small sample bias aggregated at the study level and the dependent variable level (function, pain, depression, anxiety and psychological distress). All dependent variables in this analysis were significant and at least a medium effect size: Function $d=0.65$ (95%CI 0.30 – 0.99), Pain Symptoms $d=0.85$ (95%CI 0.53 – 1.17), Depression $d=0.69$ (95%CI 0.34 – 1.04), Anxiety $d=0.66$ (95%CI 0.22 – 1.10), Psychological Distress $d=0.76$ (95%CI 0.37 – 1.14). Factors that increased effect sizes across outcomes were the number of sessions and the use of a multidisciplinary therapy. In summary, the evidence supporting the use of CBT to treat individuals with Fibromyalgia to improve functioning, decrease pain, depression symptoms, anxiety symptoms and psychological distress is strong.

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COGNITIVE BEHAVIOR THERAPY FOR FIBROMYALGIA: A META-ANALYSIS

A DISSERTATION
SUBMITTED TO THE FACULTY
OF
SCHOOL OF PROFESSIONAL PSYCHOLOGY
PACIFIC UNIVERSITY,
HILLSBORO, OREGON
BY
SUSAN M. GRITZNER
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ABSTRACT

Fibromyalgia is a chronic illness involving widespread pain, and many related symptoms such as fatigue, mood disorders, headache, and sleep disturbance. This condition has been traditionally difficult for health care providers to treat with medications. Increasingly, treatment programs for individuals with Fibromyalgia have included psychological therapies such as Cognitive Behavioral Therapy (CBT). CBT has shown preliminary evidence to support its use in Fibromyalgia; however, there is a limited understanding of CBT in this population. This meta-analysis examined all treatment studies, which included at least one group of patients receiving CBT. Functional Status, Pain Symptoms, Depression, Anxiety and Psychological distress were used as separate outcome variables to examine the effects of CBT. A literature review was conducted using Medline, PsycINFO, and the Cochrane Central Register of Controlled Trials. Of the 2000 studies that were found, 29 research studies met criteria for inclusion in the study. This resulted in 1220 participants and 167 effect sizes that could be examined. Effect sizes were corrected using Hedge's correction for small sample bias aggregated at the study level and the dependent variable level (function, pain, depression, anxiety and psychological distress). All dependent variables in this analysis were significant and at least a medium effect size: Function $d=0.65$ (95%CI 0.30 – 0.99), Pain Symptoms $d=0.85$ (95%CI 0.53 – 1.17), Depression $d=0.69$ (95%CI 0.34 – 1.04), Anxiety $d=0.66$ (95%CI 0.22 – 1.10), Psychological Distress $d=0.76$ (95%CI 0.37 – 1.14). Factors that increased effect sizes across outcomes were the number of sessions and the use of a multidisciplinary therapy. In summary, the evidence supporting the use of CBT to treat individuals with Fibromyalgia to improve functioning, decrease pain, depression symptoms, anxiety symptoms and psychological distress is strong.

INTRODUCTION

Statement of the problem

Fibromyalgia is a syndrome that involves chronic widespread pain (Wolfe et al., 1990). In addition, individuals with this syndrome experience a number of other symptoms such as sleep disturbance, fatigue, irritable bowel syndrome, headache and mood disorders (Wolfe, Ross, Anderson, Russell, & Hebert, 1995). Individuals with fibromyalgia must learn to cope with a variety of symptoms and often require significant lifestyle changes (Sarzi-Puttini, Buskila, Carrabba, Doria, & Atzeni, 2008). It is highly stressful because its etiology is not yet known, and the course of the illness is unpredictable. A further challenge for individuals with this syndrome is due to the limited effectiveness of standard treatments. Multiple treatment options are available to individuals with fibromyalgia. Available interventions include psychopharmacological treatments, physical treatments, complementary alternative medical treatments, and psychosocial treatments. Results from individual studies suggest the efficacy of these interventions is limited, both in terms of percentage of patients who improve and in terms of symptom reduction (Sarzi-Puttini et al., 2008).

Definition of Fibromyalgia

Prior to 1990, there was no generally accepted definition for the syndrome of fibromyalgia. Gombos first described fibrositis in the early 1800's as a syndrome with widespread pain. However, it was not until 1977 when Smythe and Moldofsky ignited an interest in fibrositis syndrome (Smythe & Moldofsky, 1977).

In 1990, Wolfe and other experts in this field developed the American College of Rheumatology (ACR) criteria for the classification of Fibromyalgia. The definition is reproduced here (Wolfe et al., 1990):

Figure 1. ACR criteria for a diagnosis of Fibromyalgia

1. History of widespread pain.	<p>Pain is considered widespread when all of the following are present: pain in the left side of the body, pain in the right side of the body, pain above the waist, and pain below the waist.</p> <p>In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present. In this definition, shoulder and buttock pain is considered as pain for each involved side. "Low back" pain is considered lower segment pain.</p>
2. Pain in 11 of 18 tender point sites on digital palpation.	<p>Pain, on digital palpation, must be present in at least 11 of the following 18 sites:</p> <ul style="list-style-type: none"> - Occiput: Bilateral, at the suboccipital muscle insertions. - Low cervical: bilateral, at the anterior aspects of the intertransverse spaces at C5-C7. - Trapezius: bilateral, at the midpoint of the upper border. - Supraspinatus: bilateral, at origins, above the scapula spine near the medial border. - Second rib: bilateral, at the second costochondral junctions, just lateral to the junctions on upper surfaces. - Lateral epicondyle: bilateral, 2 cm distal to the epicondyles. - Gluteal: bilateral, in upper outer quadrants of buttocks in anterior fold of muscle. - Greater trochanter: bilateral, posterior to the trochanteric prominence. - Knee: bilateral, at the medial fat pad proximal to the joint line.

- Digital palpation should be performed with an approximate force of 4 kg.
- For a tender point to be considered "positive" the subject must state that the palpation was painful. "Tender" is not to be considered "painful."
- For classification purposes, patients will be said to have fibromyalgia if both criteria are satisfied.
- Widespread pain must have been present for at least 3 months. The presence of a second clinical disorder does not exclude the diagnosis of fibromyalgia (p 171).

The authors reported that sleep disturbance, fatigue and stiffness are present in 75% of patients who meet criteria for fibromyalgia. Other symptoms such as anxiety, headaches and irritable bowel are more common in patients with fibromyalgia than in the general population.

Prevalence of Fibromyalgia

The prevalence of fibromyalgia in the United States is estimated at 5.0 million, approximately 2% of the population (Lawrence et al., 2008). This estimate is based on the only prevalence study conducted in the US in 1995 conducted in Wichita (Wolfe et al., 1995). Although no recent prevalence studies of fibromyalgia in the US have been published, a population survey of 3,395 randomly selected adults in Canada showed 100 cases of fibromyalgia, yielding an overall age/sex-adjusted prevalence of 3.3% (White, Speechley, Harth, & Ostbye, 1999). These investigators found that women are at three times the likelihood of men for having been diagnosed with fibromyalgia. Other demographic factors that increase the odds of having fibromyalgia include middle age, less education, lower household income, being divorced, and being disabled (White et al., 1999).

Mechanism of Fibromyalgia

The chronic widespread pain associated with fibromyalgia may be accounted for by dysregulatory processes in the central nervous system (CNS) (Okifuji & Turk, 1999). According to the central modulation model, dysfunctional pain mechanisms in the CNS are caused by abnormality in the neuroendocrine system, and over time may result in problematic feedback from pain to the CNS pain modulation (Yunus, 1992). Researchers have reported differences in cortisol levels, serotonin levels, somatomedin C levels and

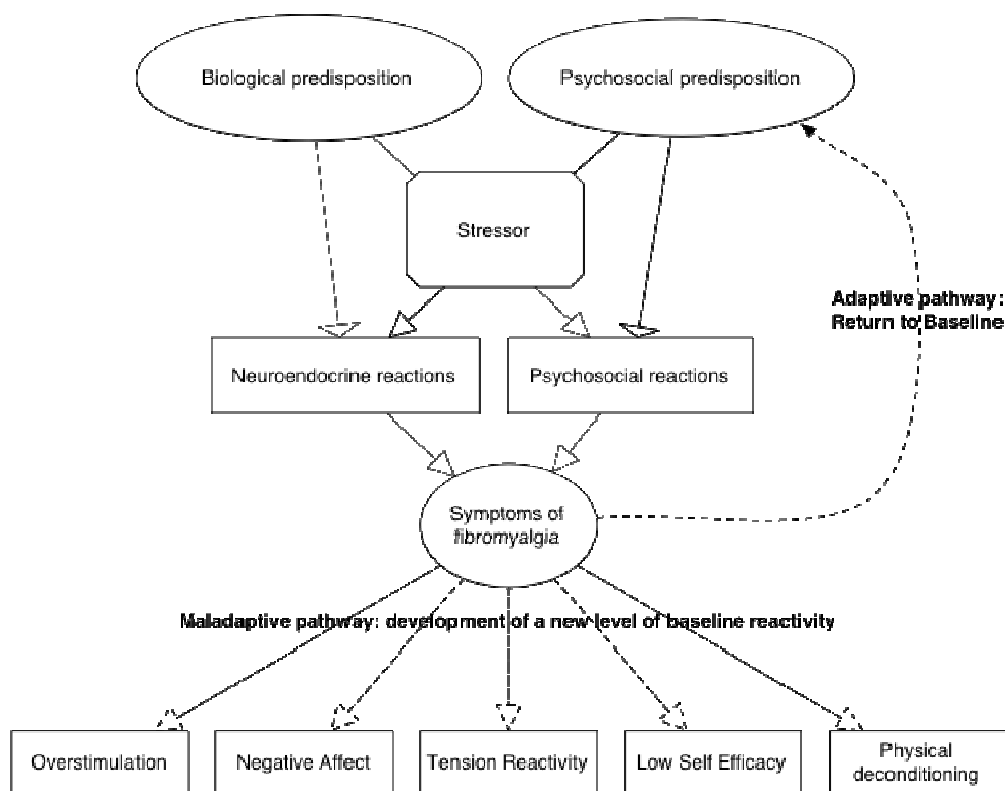
non rapid eye movement sleep between fibromyalgia patients and controls (Okifuji & Turk, 1999). Furthermore, there may be an increased level of “hypervigilance” among fibromyalgia patients, which causes a lower pain threshold and perhaps a lower threshold for perceiving fatigue (Lautenbacher & Rollman, 1997).

Recent neurobiological evidence has shed light on the neural pathways in pain processing that may be dysregulated in patients with fibromyalgia. As described by Bennett and Nelson (2006), the sensitization of the central nervous system can occur in persistent nociceptor activation, which accrues in dorsal-horn neurons. This process can be modified through the inhibitory descending pathway, which originates in the brainstem (Staud & Spaeth, 2008). This pathway is mediated by serotonin and norepinephrine. The limbic system and the frontal cortex also mediate this pathway. Thus, it is hypothesized that drugs that inhibit the reuptake of both serotonin and norepinephrine may act by stimulating the descending inhibitory pain pathway (Staud, 2002).

Okifuji and Turk (1999) describe a diathesis stress model for fibromyalgia that contains the CNS dysregulation factors but incorporates psychosocial factors as well. They hypothesize a process of physical manifestations of stress and the long-term effects of stress that take place in the body. A stressor (psychological or situational) activates the neuroendocrine and psychosocial reactions (such as increasing cortisol levels or negative affect), which are mediated by biological and psychosocial predispositions (such as genetic factors or prior learning history) and lead to symptoms (such as fatigue). In an adaptive process, the individual self-corrects and modifies their environment (uses relaxation etc.). This leads to a return to baseline levels. It is hypothesized that for some

individuals the self-corrective process does not occur. Instead, the adaptive process is blocked by dispositional factors (such as dysfunctional thoughts) or environmental factors (such as multiple significant stressors) or both. Thus, the individual is not returned to baseline, and new baseline is established which further reinforces dysregulation of the system.

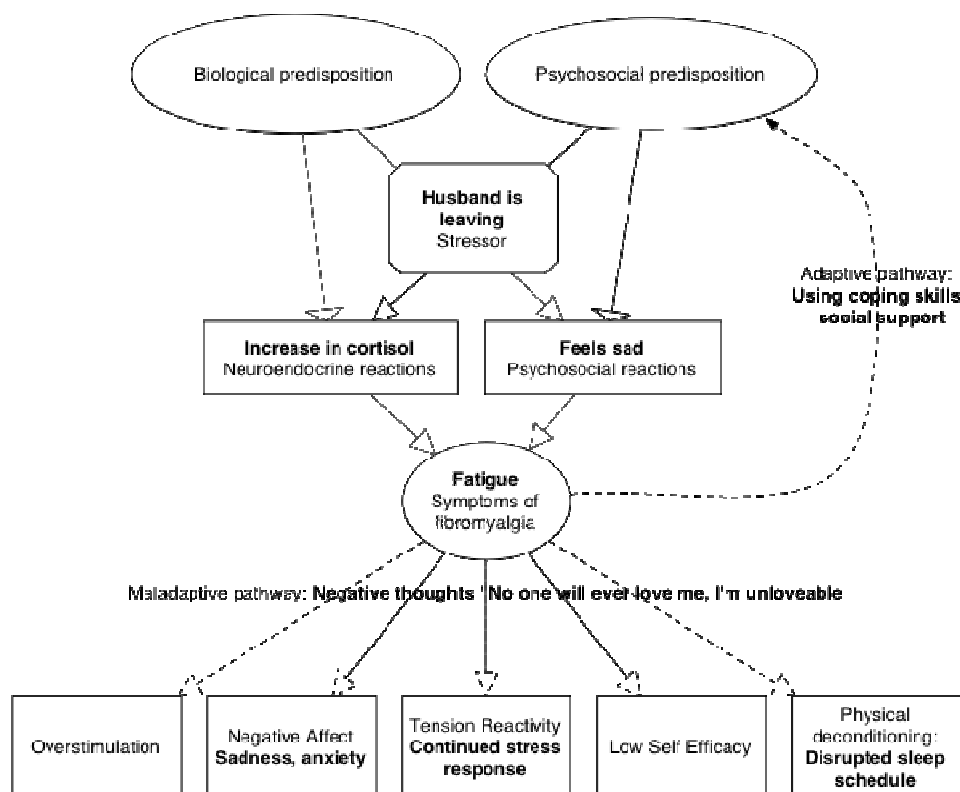
Figure 2. Diathesis stress model of Fibromyalgia



For example, a woman finds out that her husband is leaving her (stressor). Her cortisol levels rise; she worries about her future, and feels sad. This leads to difficulty sleeping and fatigue. In an adaptive process, the woman may seek support from friends; this helps her sleep, and reduces her anxiety and sadness. She can resume her sleep schedule and feel rested. Thus she can retain her baseline level of predisposition for reactivity to stressors. In a maladaptive process, the woman may think, “No one will

ever love me, I'm unlovable," and/or she may engage in a highly stressful court battle over her half of the assets. She continues to experience stress; she maintains high cortisol levels, negative emotions and disrupted sleep patterns. Thus she changes her baseline predisposition for reactivity to stressors.

Figure 3. Diathesis stress model of Fibromyalgia (with example)



These models are not mutually exclusive; they define fibromyalgia as a disorder characterized by maladaptive information processing.

Treatments for Fibromyalgia

There is no known cure for fibromyalgia; however, there are multiple treatment options. Among them are pharmacological, physical, psychological and other treatments.

Pharmacological treatments for fibromyalgia

The main pharmacological intervention that has been investigated for fibromyalgia is antidepressants. Two medications have recently been approved by the US FDA for the pharmacological treatment of fibromyalgia (Lyseng-Williamson & Siddiqui, 2008). These are an anticonvulsant (pregabalin) and an antidepressant (duloxetine). Both have been found to result in decreases in pain, anxiety and depressive symptoms in women with fibromyalgia. However, improvements from medications that decrease pain in individuals with fibromyalgia are seen independently from changes in depression and anxiety. Simple analgesics such as tramadol can also be considered in the treatment of fibromyalgia (Carville et al., 2008). Other pharmacological therapies that have been evaluated include nonsteroidal anti-inflammatories, analgesics, sedatives and anxiolytics, and corticosteroids (Forseth & Gran, 2002). These therapies have demonstrated either minimally positive effects, no effects or negative effects with patients diagnosed with fibromyalgia.

Physical treatments for fibromyalgia

Physical exercise is thought to be beneficial to patients with fibromyalgia and is directed at altering pain, fatigue, deconditioning, muscle weakness, and sleep disturbance (Forseth & Gran, 2002). Long-term participation in an exercise program has been associated with positive long-term outcomes in fibromyalgia (Wigers, Stiles, & Vogel, 1996).

Cognitive behavioral therapy for fibromyalgia

On the basis of principles originally described by Turk and colleagues (Turk, Meichenbaum, & Genest, 1983), CBT has been used in the management of chronic pain

conditions for more than two decades. The theoretical assumption underlying CBT is that thoughts, emotions and behaviors are interrelated. Following from this assumption, a change in one of these areas will produce change in the other two. Patients often present to therapy with emotion as their targeted change area. CBT typically focuses on patients' thoughts and behaviors as the mechanisms for achieving the desired change. Patients learn to identify, evaluate, and challenge unhelpful thoughts using cognitive and behavioral experiments. Core beliefs influence assumptions and trigger automatic thoughts. In addition, behaviors are thought to be maintained by the antecedents that precede them and consequences that follow them. The goal of CBT is to help clients decrease the probability that the problem behavior will occur while increasing the likelihood of an adaptive behavior. Specifically, the goals are (1) to continue the critical examination of problems, (2) to ensure that patients can execute effective coping skills in a given situation, (3) to ensure that patients learn to monitor their thoughts and behaviors during daily activities, and (4) to gradually establish new ways of thinking and responding.

CBT has been applied to clients with chronic pain (Turk et al., 1983). The CBT model supports the view that affective, behavioral, cognitive and sensory or physical aspects. These are important factors for understanding the patient's experience of pain, and emphasize the influence of the individual's beliefs on the pain experience. CBT attempts to use cognitive restructuring and behavioral experiments to reduce the inappropriate emotional responses to pain and other symptoms. This process of reducing maladaptive responses to pain sensations over time and repetition gradually results in reduced activation in neural circuitry for pain. The goals of CBT for chronic pain

typically include increasing a patients' sense of control over their pain and decreasing maladaptive thought patterns and associated behavioral improvements.

Evidence for treatments in fibromyalgia

In 1999, a meta-analysis was conducted to evaluate the effectiveness of pharmacological and non-pharmacological treatments for fibromyalgia (Rossy et al., 1999). Forty-nine studies of varying methodological quality were included and four outcome variables were included (physical status, self-report of fibromyalgia symptoms, psychological status, and daily functioning). Pharmacological treatments demonstrated improvements in physical status and self-report of symptoms; whereas, non-pharmacological treatments were overall effective in reducing physical status, self-report of symptoms, psychological status, and daily functioning. When treatments were compared, non-pharmacological treatments were more effective at improving self-report of symptoms and functional status.

Evidence for pharmacological treatments

In a meta-analytic review of 13 randomized, placebo controlled trials suggested that antidepressants improve the symptoms of fibromyalgia (O'Malley et al., 2000). Patients treated with antidepressants were more than four times as likely to improve. There appear to be mild improvements for fibromyalgia symptoms of fatigue, number of trigger points, and overall well-being; moderate improvement was found for sleep, and pain severity. The researcher reported that there was inadequate evidence to determine if a relationship exists between pharmacological treatment for fibromyalgia and improvement in depression symptoms.

Arnold, Keck, and Welge conducted a meta-analysis of the effects of tricyclic antidepressant on the symptoms of fibromyalgia (Arnold, Keck, & Welge, 2000). They found that tricyclics had a moderate effect on these symptoms. In particular, these medications were found to have the highest effect on sleep symptoms. Moderate effects were also found for pain, functioning and for tender points. This study did not examine the effects of antidepressants on symptoms of anxiety and depression.

A recent meta-analysis of antidepressant effects on fibromyalgia was conducted (Hauser, Bernardy, Uceyler, & Sommer, 2009). Researchers examined randomized controlled trials of tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin and noradrenaline reuptake inhibitors (SNRIs), and monoamine oxidase inhibitors (MAOIs) found that there was evidence for an association of antidepressants with moderate reduction in pain, and small reductions in fatigue, depressed mood, and sleep disturbances. Effect sizes for pain reduction were large for TCAs medium for MAOIs and small for SSRIs and SNRIs.

Tramadol is a centrally acting analgesic medication. It has a dual effect of being a weak opioid and it inhibits the reuptake of serotonin and noradrenaline. Recent randomized controlled trials of tramadol have shown decreases in pain in patients with fibromyalgia (Bennett, Kamin, Karim, & Rosenthal, 2003; Russell et al., 2000). The use of analgesics in patients with fibromyalgia could be used with some caution due to the possibility of opiate withdrawal effects and tolerance (Carville et al., 2008).

Evidence for physical treatments

A recent comprehensive review of literature on exercise therapy for fibromyalgia

was in support of physical exercise as a treatment for fitness and improvement in symptoms (Jones, Adams, Winters-Stone, & Burckhardt, 2006). The researchers reviewed forty-six studies that examined a standardized exercise program in patients with fibromyalgia. They examined studies that looked at visual analogue scales of symptoms, health and impact questionnaires. Subjects achieved symptom relief, particularly decreased pain and fatigue as well as improved sleep and mood, with low to moderate intensity exercise of any type. In general, the greatest effect and lowest drop out rates occurred in exercise programs that were of lower intensity than those of higher intensity.

A recent meta-analysis was conducted to examine the effects of multicomponent treatment in fibromyalgia (Hauser, Bernardy, Arnold, Offenbacher, & Schiltenswolf, 2009). Multicomponent therapies include at least one exercise therapy and at least one psychological or educational therapy. Nine studies that met these criteria were included in the analysis. Researchers found that interventions that combined physical and psychological interventions were effective in significantly reducing pain, depression and increases quality of life. The most dramatic effects of these interventions were for depressed mood and fatigue. Pain and physical fitness effect sizes were small to moderate, but significant.

Evidence examining CBT in Fibromyalgia

Neilson and his colleagues conducted the first investigation of using CBT in patients with fibromyalgia (Nielson, Walker, & McCain, 1992). They administered a comprehensive cognitive behavioral treatment that included relaxation, cognitive techniques, aerobic exercise, pacing strategies, family education, a return to home and community activities and medication management. Patients were assessed both pre and

post intervention times and improvement was seen in the areas of pain severity, emotional distress, anxiety, depression, and life interference (functional status). However, improvement was not statistically significant for patients on overall activity level. Two years later, a follow-up study was done to investigate the long-term benefits of this type of treatment in patients with fibromyalgia. Control over pain, worry and observed pain behavior continued to show a significant decrease from baseline levels.

Vlaeyen and colleagues examined a cognitive educational treatment for fibromyalgia using a randomized control trial (Vlaeyen et al., 1996). In their sample, the patients had significant disability. The majority of patients was unemployed, fearful, and had experienced pain symptoms for an average of ten years. The majority of patients did not experience significant treatment reductions in symptoms as a result of the treatments. The cognitive educational group showed significant improvements in pain coping and pain control; however, they did not show statistically significant improvements in pain behavior, pain intensity, activity levels, depression or anxiety.

Patients with fibromyalgia were randomly assigned to either an aerobic exercise program, a stress management program, or treatment as usual (Wigers et al., 1996). Patients in both the aerobic exercise group and the stress management group showed a statistically significant reduction in their dolorimeter score, which assesses the tender points. The majority of clients did not experience significant symptoms (pain, depression, and functional activities) reduction at the end of the treatment period. The aerobic exercise interventions lead to a reduction of symptoms; however, few patients continued the treatment at follow up. At follow up, the majority of patients had

continued the stress management daily or twice weekly. In particular, 69% continued with relaxation strategies in spite of “no effects.”

Behavioral and education/control interventions in a group format were evaluated in the treatment of 72 men and women with fibromyalgia (Nicassio et al., 1997). Groups met for 90 minutes each week for 10 weeks. The investigators found that there were improvements across time for both groups, but that there was no difference between groups in that. Significant reductions in depression, self-reported pain behavior, observed pain behavior, and myalgia scores occurred. However, changes in function and well-being did not occur over the course of the trial.

Buckelew and her colleagues examined the effects of a therapy comparing biofeedback and relaxation to exercise and a combination of the two (Buckelew et al., 1998). All three groups showed an increase in self-efficacy for function. The relaxation and biofeedback group showed short-term improvements in pain scores. Furthermore, depression did not change in the short-term but showed significant improvement in the two-year follow up period. The exercise and combination groups obtained modest improvements on the physical activity score. The investigators also found support for the hypothesis that treatment may prevent the development of increased tender spots in untreated individuals. In the long term, only the combination group continued to show an increase in self-efficacy for function.

Another group compared EMG biofeedback to sham-biofeedback as a treatment for individuals with fibromyalgia (Babu, Mathew, Danda, & Prakash, 2007). Patients were randomized to receive 6 days of 45-minute sessions of either biofeedback or sham biofeedback, which consisted of an alteration of the visual feedback provided to the

client, irrespective of their muscle activity. The authors found that there were significant decreases in functional status, pain, and number of tender points in the group that received biofeedback. This study did not examine depression or anxiety.

These researchers compared standard medication treatment including pharmacological interventions and suggestions for exercise with and without the addition of a brief intensive cognitive behavioral intervention (Williams et al., 2002). This intervention was specifically targeted at increasing physical function. Results indicate that physical function improved. Depression and anxiety measures were not reported. Pain was unaffected by the addition of the intervention. This is consistent with the pain literature in that pain is not consistently associated with physical function.

Patients with fibromyalgia were randomized to receive operant behavioral treatment or physical therapy (Thieme, Gromnica-Ihle, & Flor, 2003). Significant improvements were found in the operant group on dependent measures of pain intensity, interference, affective distress (depression and anxiety), self-efficacy, spousal response to pain, medication intake and pain behaviors. These improvements were demonstrated in spite of concurrent reduction in medication intake. No improvements were found for total activities. The physical therapy and medication management comparison group deteriorated in almost all variables measured.

Fifty-six fibromyalgia patients were randomly assigned to participate in either a cognitive behavioral or physical exercise based therapy (Redondo et al., 2004). Patients in the exercise group demonstrated improvement in physical activity, but not in functional status (common finding). Patients in the CBT groups demonstrated improvement in functional status as well, but not in terms of depression, anxiety or self-

efficacy. CBT increased the use of strategies to manage pain such as relaxation. Neither group reported significant decreases in pain.

CBT was examined in a sample of adolescents with fibromyalgia (Redondo et al., 2004). The patients were randomly assigned to either an 8-week CBT group or 8 weeks of self-monitoring. At week 8, both groups showed a decrease in depression and functional disability. Patients who received CBT showed significant ability to cope with pain and a trend towards decreased pain intensity; however, there was no objective decrease in pain for either group. Those in the self-monitoring group followed by the CBT group seemed to receive the most benefit.

These investigators examined the differential effects of psychopharmacological (amitryptiline or cyclobenzapine) interventions, CBT, and CBT and pharmacological interventions combined on patients with fibromyalgia (Garcia, Simon, Duran, Cancellor, & Aneiros, 2006). CBT decreased fibromyalgia symptoms in both post treatment and follow up time periods. Interestingly, the CBT and psychopharmacological approached did not show similarly significant improvements in symptoms. Number of tender points trended towards improvement in the CBT group. Depression and anxiety were measured initially but were not followed up after treatment because a physician conducted blinded follow up assessments of FIQ and number of tender points.

Hammond and Freeman (2006) compared a patient education program combined with exercise to a relaxation group. Short-term benefits from the education and exercise group are evident; however, long-term benefits were not sustained (Hammond & Freeman, 2006). Doctors' visits were reduced in both groups these changes were maintained over time. No changes in depression and anxiety were reported.

Furthermore, reports of pain did not significantly improve in either group. The authors identified additional treatment components that may have improved the effectiveness of the treatments. They recommended motivational interviewing, home-based treatment, and more homogeneous groups of patients.

A quasi-experimental study was conducted to examine the effectiveness of group therapy specifically targeted towards promoting adaptive active coping skills on a cognitive, behavioral, and emotional level in patients with fibromyalgia (Anderson & Winkler, 2007). The investigators found significant improvements in depression, pain, and fatigue. Overall, the treatment group experienced an improvement in functioning. Anxiety was not monitored in this study.

Mindfulness-based therapies are a recent development in the treatment of chronic pain (Kabat-Zinn, Lipworth, & Burney, 1985). Researchers have attempted to compare the use of a mindfulness based stress reduction (MBSR) treatment program to standard treatment for individuals with fibromyalgia (Sephton et al., 2007). The MBSR group had significantly reduced depressive symptoms. This study did not report changes in anxiety, physical functioning or pain.

One hundred and twenty five patients with fibromyalgia were randomly assigned to participate in operant behavioral and cognitive behavioral therapies (Thieme, Flor, & Turk, 2006). The cognitive group focused on changing maladaptive cognitions associated with pain and providing coping strategies. The operant group focused on changing observable pain behaviors and utilized punishment and reinforcement. Both groups demonstrated significant improvement in a one-year follow up period as compared to an attention control group. Furthermore the attention control group which

consisted of a discussion of symptoms and problems caused by fibromyalgia resulted in a 50% drop out rate and an increase in symptoms. In particular, improvements were seen in functional status, and pain intensity. Affective distress (which captures depression and anxiety) did not show significant reductions for either group.

As a follow up study to the study by Thieme, Flor and Turk (2006), this group considered specific patient characteristics that responded well to treatment in the trial. In particular, the authors conducted a multiple regression analysis to determine which patient characteristics would predict improvement in pain intensity and physical impairment (Thieme, Turk, & Flor, 2007). The authors found that patients responded to both treatments in terms of decreasing physical impairment if they had a higher initial physical impairment, lower initial affective distress, higher initial pain behaviors and reduced solicitous spousal behavior. The authors found that patients responded to both treatments in terms of decreasing pain intensity if they had lower initial physical impairment. Of note, psychological variables did not predict reductions in pain.

Two literature reviews regarding the use of CBT for patients with patients with fibromyalgia have been published (Bennett & Nelson, 2006; van Koulil et al., 2007). Bennett and Nelson (2006) found that CBT does not provide sustained pain relief to patients with fibromyalgia. The primary function of CBT for patients with fibromyalgia is related to improvements in areas other than pain. Specifically, these reviewers concluded that we should look to CBT to provide improvements in self-efficacy, dysfunctional thought patterns and physical functioning.

The second review was conducted to examine the effects of CBT, exercise programs or the combination of the two (van Koulil et al., 2007). The authors reported

that multimethod treatments were more effective than specific CBT components provided. However, effects from both treatments tended to disappear in the long term. They further suggested that outcomes might be improved if there were opportunities to specifically target specific groups of patients within the group of fibromyalgia patients.

One potential reason for some of the inefficiencies found in treatment programs could be the heterogeneity of patients in the groups. In their article of 1996, Turk and his colleagues investigated a group of patients with fibromyalgia using structural equation modeling to determine if patients could be separated into subgroups based on psychosocial and behavioral responses to pain (Turk, Okifuji, Sinclair, & Starz, 1996). They found that there were three groups of patients that could be grouped together. The dysfunctional group is characterized by poor coping and high level of pain, the interpersonally distressed group is characterized by interpersonal difficulties, and low pretreatment levels of affective distress and disability characterize the adaptive coper group. One study examined how these groups respond to standard interdisciplinary treatment for fibromyalgia (Turk, Okifuji, Sinclair, & Starz, 1998). The dysfunctional group experienced statistically significant reductions in pain, affective distress, perceived disability, and perceived interference of pain. The interpersonally distressed group was not responsive to this treatment. The adaptive coper group experienced significant reductions in pain, but did not show reductions in their already low levels of functional disability and affective distress. The authors emphasized using customized treatment programs based on the patients' psychosocial and behavioral responses to pain and hypothesized that this will lead to improved outcomes in treatments.

A group of researchers from the Netherlands utilized a case study design to better understand the effects of customizing treatment for different groups of patients (van Koulil et al., 2008). They differentiated between patients with fibromyalgia based on two patterns of psychosocial and behavioral responses to pain: the pain-avoidant pattern and the pain-persistence pattern. The pain avoidant pattern is best characterized by a high level of pain avoidance behaviors, preoccupation with painful stimuli, pain related worrying, and fear of pain or movement. The pain persistence pattern is characterized by a low level of pain avoidance behavior, activity in spite of pain, ignoring pain a physical limits, and non-acceptance and demanding cognitions about limitations. The therapeutic approach that was useful with a patient who is characterized by a pain-avoidant pattern was aimed at diminishing fear of pain and increasing the level of daily activity. The therapeutic approach that was useful with a patient who is characterized by a pain-persistence pattern was aimed at changing pain-persistence cognitions and achieving a regulation of daily activities.

HYPOTHESES

Studies examining the effects of CBT in patients with fibromyalgia will demonstrate effectiveness of the treatment for outcomes of pain, functioning, depression, anxiety and psychological distress.

1. CBT will improve the symptoms of pain in individuals with fibromyalgia between pre- and post CBT treatment.
2. CBT will improve the functioning in individuals with fibromyalgia between pre- and post CBT treatment.
3. CBT will improve the symptoms of depression in individuals with fibromyalgia between pre- and post CBT treatment.
4. CBT will improve the symptoms of anxiety in individuals with fibromyalgia between pre- and post CBT treatment.
5. CBT will improve the symptoms of psychological distress in individuals with fibromyalgia between pre- and post CBT treatment.

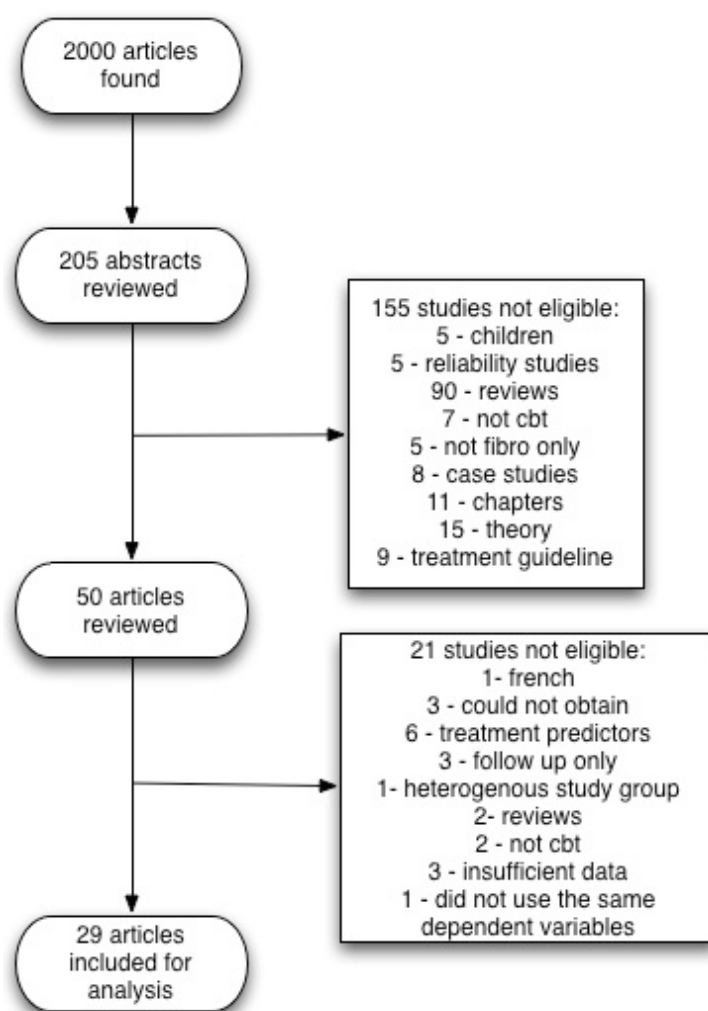
METHOD

Study retrieval

The electronic bibliographic databases screened included Medline (1950 through August 2009), PsycINFO (1950 through August 2009), and the Cochrane Central Register of Controlled Trials (1993 through August 2009). Dates were chosen to be most inclusive of potential studies. The keywords used in the initial inclusion were “fibromyalgia” and “fibromyalgia syndrome” in combination with “cognitive behavioral therapy,” “cognitive therapy,” and “behavior therapy.” In addition, reference sections of original studies and review papers on cognitive behavioral therapy for fibromyalgia were screened manually by the author (SG). Only studies in English were included. Of the 2000 studies that were found using this search, 205 of the abstracts were reviewed for the study based on their mention of fibromyalgia in their abstract. Of the 205 abstracts, 155 were determined to be ineligible for the study (See Figure 4), and 50 were included for more in-depth review by the author. Of the 50 that were included for review, the author could not obtain 3 of the articles, 1 article was in French, 1 article was a duplicate and 21 articles were determined to be ineligible for the study (See Figure 4). Twenty-nine articles remained and were included in the study. Of the 29 studies, 3 had two groups that could be examined in this study (CBT, and CBT and hypnosis, cognitive therapy and operant behavior therapy, and pain-avoidance treatment and pain-persistence treatment) this resulted in a total of 32 groups that were examined in the meta-analysis (Anderson & Winkler, 2007; Burckhardt, Clark, O'Reilly, & Bennett, 1997; Castel, Salvat, Sala, & Rull, 2009; Creamer, Singh, Hochberg, & Berman, 2000; Edinger, Wohlgemuth, Krystal, & Rice, 2005; Falcao et al., 2008; Fors & Gotestam, 2000; Garcia et al., 2006;

Goldenberg et al., 1994; Hammond & Freeman, 2006; Keel, Bodoky, Gerhard, & Muller, 1998; Kroese et al., 2009; Lera et al., 2009; Lumley et al., 2008; Menzies & Kim, 2008; Menzies, Taylor, & Bourguignon, 2006; Nicassio et al., 1997; Nielson et al., 1992; Sephton et al., 2007; Shapiro, Anderson, & Danoff-Burg, 2005; Singh, Berman, Hadhazy, & Creamer, 1998; Suman et al., 2009; Thieme et al., 2006; Thieme et al., 2003; van Koulil et al., 2010; Vazquez-Rivera et al., 2009; Vlaeyen et al., 1996; Wigers et al., 1996; Williams et al., 2002).

Figure 4. Flow diagram of literature review and application of inclusion and exclusion criteria.



Inclusion and Exclusion Criteria

To be included in the analysis, studies were required to meet the following criteria:

1) the study included at least one group receiving cognitive therapy or behavioral therapy or some combination, 2) the diagnosis of fibromyalgia has to be based on recognized criteria (e.g., Wolfe et al., 1990 criteria, ACR criteria), 3) the study had to report pre- and post- measures for their treatment group, 4) the study had symptom specific outcomes of the keys symptoms of fibromyalgia, such as pain, fatigue, depressive symptoms, and health related quality of life, and/or relevant pain-related psychological domains, and/or objective tests of physical fitness, 5) the study was published in full paper form, and 6) data was suitable for meta-analysis (e.g., appropriate numerical information needed to calculate effect size such as number of participants in the treatment group, means and standard deviations pre- and post-treatment). In three studies estimations were used to compute effect sizes. One study was excluded due to incomplete data (i.e., only baseline scores and standard deviations and t-scores looking at the difference in scores between treatment successes and treatment failures, not post treatment scores were available) presented in the article; the author (SG) attempted to contact these authors, but was unable to make contact. Studies were excluded from the analysis on the basis of the following criteria: 1) The use of ONLY psychoeducation for treatment, 2) the use of ONLY relaxation for treatment, 3) the use of a non-adult (under age 18) sample, 4) studies examining follow up, intent to treat, or adherence only, i.e., no pre-post data for analysis (as above).

Coding Manual

Codes were both developed for the present study and taken from the example in the book *Practical Meta-analysis* (Lipsey & Wilson, 2001). Appendix A presents details of codes. Effect sizes were computed independently of other coding to avoid bias that might result from knowing outcomes. A description of the variables coded in the study follows (Please see appendix A for full Coding Manual used).

Sample descriptors – Four sample descriptors were used: (a) mean age of the sample, (b) predominant sex of sample, (c) average duration of fibromyalgia symptoms in the sample, (d) whether or not medications were being used by the sample.

Research design descriptors – Four research design descriptors were used: (a) type of treatment (b) scientific integrity of the research design, (c) initial treatment group size, (d) follow-up treatment size, and (e) attrition.

Nature of treatment descriptors – Three of treatment descriptors were used: (a) CBT components of the treatment (each component of CBT was graded separately and indicated if present vs. not present), (b) duration/length of the treatment, and (c) time until follow up.

Dependent variables – Four dependent variables were used: (a) functional ability, (b) pain, (c) depression, and (d) anxiety. The type of scale used was also coded for analysis. Following data collection, one additional dependent variable was added called (e) level of distress, and was distinguished from measures that looked exclusively at depression and negative mood. Each measure used in the studies was coded as one of these five dependent variables, and codes are provided for those in the coding manual.

Effect sizes – Eight effect size variables were used: (a) page number, (b) treatment group size, (c) mean pre-intervention, (d) standard deviation pre-intervention, (e) mean post-intervention, (f) standard deviation post-intervention, (g) effect size, (h) raw difference.

Statistical Analysis

Reliability Analysis

Interrater reliability

A reliability analysis was conducted in which two graduate students coded six variables within all studies independently. Four continuous variables, pre-treatment means and standard deviations, post-treatment means and standard deviations of all 167 effect sizes and two categorical variable, type of dependent variable (function, pain, depression, and anxiety) and specific for the dependent variable were selected for the reliability study.

A Pearson correlation was computed for the continuous variables; the pre-treatment mean ($r = .95$), the pre-treatment standard deviation ($r = .99$), the post-treatment mean ($r = .96$), the post-treatment standard deviation ($r = .99$). The results indicated a high level of agreement between raters with respect to the pre and post treatment means and standard deviations. A coefficient kappa was computed for both of the categorical variables; type of dependent variable ($K = .97$), and specific type of dependent variable ($K = .85$). According to Fleiss, both values represent excellent agreement beyond chance (Fleiss, 1981). The disagreement between coders was resolved by the author by examining each disagreement and comparing it to the original article. No changes were made to the coding manual as a result of this analysis.

Intra-rater reliability

A reliability analysis was conducted by the author on 10% on the studies for all of the study variables, which was done to ensure consistency and quality of coding by the author. The studies were randomly selected. All variables in the study were examined. Sixteen continuous variables were examined using Pearson correlations (age, sex, duration of illness, N at baseline, N at follow up, weeks of treatment (weeks), number of sessions, length of sessions (minutes), time to first follow up(months), time to second follow up (months), size of the treatment group, pre-treatment means and standard deviations, post-treatment means and standard deviations) and 7 categorical variables were examined using coefficient kappa (diagnostic criteria used, medications, type of therapy delivery, scientific quality and type of dependent variable (function, pain, depression, anxiety, and psychological distress), specific type of the dependent variable and raw score difference (improvement, decline, no change)). Results of the intra-rater reliability study are presented in Table 1. Overall, these results indicated a moderate to high level of intra-rater reliability. All discrepancies were reviewed by the author, and compared to the original article for confirmation.

Table 1. Intra-rater reliability with 10% of the studies included in the analysis (n =11)

Continuous Variables	<i>r</i>	Categorical Variables	<i>K</i>
Age	0.98	Diagnostic Criteria	0.74
Sex	0.97	Medications	0.72
Duration of Illness	0.96	Type of Therapy	1.00
Baseline (<i>n</i>)	1.00	Scientific Quality	0.84
Follow-up (<i>n</i>)	1.00	Dependent Variable	0.96
Weeks of Treatment (weeks)	1.00	Dependent Variable (Specific)	0.91
Number of Sessions	1.00	Score Difference (Raw)	0.90
Length of Sessions (minutes)	1.00		
Time to first follow-up (months)	1.00		
Time to Second Follow-up (months)	1.00		
Treatment Group (Size)	1.00		
Pre-treatment (mean)	1.00		
Pre-treatment (<i>SD</i>)	1.00		
Post-treatment (mean)	1.00		
Post-treatment (<i>SD</i>)	0.99		

Effect Size Calculation

Effect sizes were calculated for this meta-analysis using the standardized mean difference statistic. When possible, effect sizes will be calculated directly using this formula:

$$d = \frac{X_{\text{post}} - X_{\text{pre}}}{s_p}$$

where X_{pre} is the mean score of the treatment group prior to receiving treatment and X_{post} is the mean of the score of the treatment group following treatment, and s_p is the pooled

standard deviations. When this information was not reported I estimated d using an effect size calculator (Shadish, Robinson, & Lu, 1999).

Statistical analysis

First, the effect sizes were corrected using Hedge's correction for small sample bias in the standardized mean difference effect size (Hedges, 1981). The effect sizes were then aggregated at the study level and the dependent variable level (function, pain, depression and anxiety) and descriptive statistic analyses including the quartiles, means, standard deviations and the range were performed (for both aggregated data and non-aggregated data). Using Hoaglin's method to determine upper bound and lower bound outliers (Hoaglin, Iglewicz, & Tukey, 1986). Thirteen outliers were found. After careful consideration of each outlier, all outliers were kept for the analysis; a detailed analysis of all outliers is noted below for each dependent variable. Combined effect sizes and associated statistics were computed such as the weighted mean effect size, the conditional variance of effect size, and the confidence intervals around the effect sizes. Homogeneity analyses were conducted on the effect sizes for each dependent variable level. In light of the inclusion criteria identified for this study including a wide range of eligible studies, it was pre-determined that the study would be carried out using the random effects model, due to the ability of this model to adjust for both subject level variance, but also study level variance.

The meta-analysis analog to the analysis of variance was conducted to determine how much variance in effect sizes is due to categorical variables that were thought to impact the average effect size. Level of scientific quality and type of CBT treatment (Individual, group, multidisciplinary) were used because they were both thought to have

impacted the average effect size. Furthermore, the weighted regression analysis was performed to determine how much of the variance in effect sizes is due to continuous variables. The continuous variables investigated here were the length of CBT sessions, the duration of treatment, the number of CBT treatments used, and attrition.

RESULTS

Descriptive Results

Twenty-nine studies were included in the meta-analysis for review, the total sample size across all the studies reviewed was $n = 1220$. As previously indicated, three studies had two groups that were examined, this resulted in 32 groups. The average age of participant across groups was 45.6 (SD 8.5), the average percentage of female gender was 95.6%, and the average duration of fibromyalgia symptoms was 7.95 years. On average CBT treatment took an average of 9.8 weeks, 13.1 sessions, and sessions were 121.9 minutes in length. Each group included some component of CBT, and Table 2 indicates the percentage of studies that contained each component of CBT.

The effect sizes were first examined to determine if the data contained any outliers. Effect sizes after aggregation for all studies had a lower bound for outliers of -0.77 , and an upper bound of 1.96 . Thirteen effect sizes fell outside this range from $d = 2.08$ to $d = 5.52$; they were included in subsequent analyses because upon examination, they were confirmed to meet inclusion criteria for the study and no errors were found. Of the 169 effect sizes computed, after aggregation there were twenty-two study-level effect sizes for functional status, thirty-one study-level effect sizes for pain, seventeen study-level effect sizes for depression, fourteen study-level effect sizes for anxiety and twelve study-level effect sizes for psychological distress. Next, the distribution of effect sizes for the studies was analyzed by the dependent measure.

Table 2. Description of Cognitive Behavioral Therapy components (n = 32)

CBT Components	Percent of groups containing the specific component
Relaxation Training	87.5
Psychoeducation	81.3
Homework	78.1
Chronic Pain Self-management	78.1
Self-monitoring	68.8
Stress Management	65.6
Cognitive Restructuring	59.4
Exercise	37.5
Exposure/Behavior Modification	28.1
Pleasant Activity Scheduling	28.1
Problem Solving	25.0
Support Person Involvement	25.0
Assertiveness Training and/or Social Skills Training	25.0
Biofeedback	12.5
Sleep Hygiene	12.5
CBT = Cognitive Behavioral Therapy	

Functional status

After aggregation there were twenty-two effect sizes for the dependent measure functional status which ranged from $d = 0.00$ to $d = 3.95$ with a mean of 0.64. Effect sizes for functional status had a lower bound for outliers of -0.57 , and an upper bound of 1.46. One effect size fell outside this range, $d = 3.95$. A homogeneity analysis was conducted and the results indicated a heterogeneous distribution ($\chi^2(22) = 241.05$, $p < 0.001$). The null hypothesis for homogeneity was rejected suggesting that it cannot be

assumed that the data contains only subject level variability, but also some study level variability, and indicating the use of a random effects model.

The mean effect size of the random effects model was $d = 0.65$ ($SE = 0.17$). Also, the confidence intervals were wider under the random effects model because the between-study variability is added to sampling error variability and thus increases the uncertainty associated with the estimate of the population mean. The mean effect size was found to be significantly different from zero.

The mean effect size for the sample of studies under the random effects model was 0.65 ($SE = 0.18$) and was statistically significant ($z = 3.68$, $p = 0.0002$). The 95% confidence interval around the mean effect size ($0.30 < \mu < 0.99$) did not include zero and reveals the relevant precision of the estimate of the mean effect size. The variance component for the random effects analysis is 0.63 indicating that approximately 63% of the variance is not accounted for by sampling error.

Several analyses were conducted to test the ability of several categorical and continuous variables to explain the excess effect size variability. Results of these analyses are summarized in Tables 3 and 4. For functional status, scientific quality, type of CBT treatment, number of CBT components, number of weeks, and attrition rates did not significantly contribute to the variability in functional status. Number of sessions did account for 29% of the variance ($R^2 = 0.30$, $p = 0.003$) in effect sizes for functional status.

Pain

After aggregation there were thirty-one effect sizes for the dependent measure pain which ranged from $d = 0.10$ to $d = 4.5$ with a mean of 0.85 . Effect sizes for pain had a lower bound for outliers of -0.43 , and an upper bound of 1.74 . Two effect sizes fell

outside this range, $d = 2.75$ and $d = 4.50$. A homogeneity analysis was conducted and the results indicated a heterogeneous distribution ($\chi^2 (30) = 319.94, p < 0.001$). The null hypothesis for homogeneity was rejected suggesting that it cannot be assumed that the data contains only subject level variability, but also some study level variability, and indicating the use of a random effects model.

The mean effect size for the sample of studies under the random effects model was 0.85 ($SE = 0.16$) and was statistically significant ($z = 5.18, p < 0.001$). The 95% confidence interval around the mean effect size ($0.53 < \mu < 1.17$) did not include zero and reveals the relevant precision of the estimate of the mean effect size. The variance component for the random effects analysis is 0.73 indicating that approximately 73% of the variance is not accounted for by sampling error.

Several analyses were conducted to test the ability of several categorical and continuous variables to explain the excess effect size variability. Results of these analyses are summarized in Tables 3 and 4. For pain, scientific quality, number of CBT components, number of weeks, and attrition rates did not significantly contribute to the variability in pain. Number of sessions did account for 29% of the variance ($R^2 = .29, p = 0.001$) in effect sizes for pain. For the random model the value of the variance component for type of CBT treatment was statistically significant, $Q (2) = 11.13, p = 0.004$. Studies using individual CBT ($n = 4$) had a mean $d = .60$ ($SE = 0.49$) and a 95% confidence interval of -0.35 to 1.56, which was not significantly different from group CBT ($n = 25$) having a mean $d = 0.67$ ($SE = 0.16$) and a 95% confidence interval of 0.36 to 0.98; however, multidisciplinary CBT treatment ($n = 5$) was significantly different from

both having a mean of $d = 2.01$ ($SE = 0.38$) and a 95% confidence interval of 1.27 to 2.74.

Depression

After aggregation there were seventeen effect sizes for the dependent measure depression which ranged from $d = -0.10$ to $d = 2.67$ with a mean of 0.69. Effect sizes for depression had a lower bound for outliers of -0.68 , and an upper bound of 1.95. One effect size fell outside this range, $d = 2.66$. A homogeneity analysis was conducted and the results indicated a heterogeneous distribution ($\chi^2(17) = 153.72, p < 0.001$). The null hypothesis for homogeneity was rejected suggesting that it cannot be assumed that the data contains only subject level variability, but also some study level variability, and indicating the use of a random effects model.

The mean effect size for the sample of studies under the random effects model was 0.69 ($SE = 0.18$) and was statistically significant ($z = 3.85, p = 0.0001$). The 95% confidence interval around the mean effect size ($0.34 < \mu < 1.04$) did not include zero and reveals the relevant precision of the estimate of the mean effect size. The variance component for the random effects analysis is 0.50 indicating that approximately 50% of the variance is not accounted for by sampling error.

Several analyses were conducted to test the ability of several categorical and continuous variables to explain the excess effect size variability. Results of these analyses are summarized in Tables 3 and 4. For depression, scientific quality, number of CBT components, number of weeks, and attrition rates did not significantly contribute to the variability in depression. Number of sessions did account for 21% of the variance

($R^2=.21$, $p = 0.01$) in effect sizes for depression. For the random model the value of the variance component for type of CBT treatment was statistically significant $Q(1) = 6.98$, $p = 0.04$. Studies using group CBT ($n= 15$) had a mean $d = 0.51$ ($SE = 0.15$) and a 95% confidence interval of 0.22 to 0.81, which was significantly different from multidisciplinary CBT ($n= 3$) having a mean $d = 1.46$ ($SE = 0.32$) and 95% confidence interval of 0.82 to 2.09.

Anxiety

After aggregation there were fourteen effect sizes for the dependent measure anxiety which ranged from $d = -0.12$ to $d = 2.99$ with a mean of 0.63. Effect sizes for anxiety had a lower bound for outliers of -0.91 , and an upper bound of 1.89. One effect size fell outside this range, $d=2.67$. A homogeneity analysis was conducted and the results indicated a heterogeneous distribution ($\chi^2(14) = 166.06$, $p < 0.001$). The null hypothesis for homogeneity was rejected suggesting that it cannot be assumed that the data contains only subject level variability, but also some study level variability, and indicating the use of a random effects model.

The mean effect size for the sample of studies under the random effects model was .66 ($SE = .23$) and was statistically significant ($z = 2.92$, $p = 0.035$). The 95% confidence interval around the mean effect size ($0.22 < \mu < 1.10$) did not include zero and reveals the relevant precision of the estimate of the mean effect size. The variance component for the random effects analysis is 0.69 indicating that approximately 69% of the variance is not accounted for by sampling error.

Several analyses were conducted to test the ability of several categorical and continuous variables to explain the excess effect size variability. Results of these

analyses are summarized in Tables 3 and 4. For anxiety, scientific quality, number of CBT components, number of weeks, and attrition rates did not significantly contribute to the variability in anxiety. Number of sessions did account for 29% of the variance ($R^2=0.29$, $p = 0.02$) in effect sizes for anxiety. For the random model the value of the variance component for type of CBT treatment was statistically significant $Q(1) = 5.94$, $p = 0.015$. Studies using group CBT ($n= 13$) had a mean $d = 0.44$ ($SE = 0.19$) and a 95% confidence interval 0.07 to 0.82, which was significantly different from multidisciplinary CBT ($n= 4$) having a mean $d = 1.47$ ($SE = 0.37$) and a 95% confidence interval of .74 to 2.20.

Psychological distress

After aggregation there were twelve effect sizes for the dependent measure psychological distress which ranged from $d = -0.10$ to $d = 2.67$ with a mean of .81. Effect sizes for psychological symptoms had a lower bound for outliers of -0.89 and an upper bound of 2.26. One effect size fell outside this range, $d = 2.67$. A homogeneity analysis was conducted and the results indicated a heterogeneous distribution ($\chi^2(11)=57.24$, $p < 0.001$). The null hypothesis for homogeneity was rejected suggesting that it cannot be assumed that the data contains only subject level variability, but also some study level variability, and indicating the use of a random effects model.

The mean effect size for the sample of studies under the random effects model was 0.76 ($SE = 0.20$) and was statistically significant ($z = 3.84$, $p = 0.0001$). The 95% confidence interval around the mean effect size ($0.37 < \mu < 1.14$) did not include zero and reveals the relevant precision of the estimate of the mean effect size. The variance

component for the random effects analysis is 0.35 indicating that approximately 35% of the variance is not accounted for by sampling error.

Several analyses were conducted to test the ability of several categorical and continuous variables to explain the excess effect size variability. Results of these analyses are summarized in Tables 3 and 4. For psychological distress, scientific quality, number of CBT components, and attrition rates did not significantly contribute to the variability in depression. Number of sessions did account for 38% of the variance ($R^2=0.38, p = 0.01$) in effect sizes for psychological distress. Number of weeks of treatment did account for 38% of the variance ($R^2=0.38, p = 0.01$) in effect sizes for psychological distress. For the random model the value of the variance component for type of CBT treatment was statistically significant $Q(2) = 5.47, p = 0.04$. Studies using individual CBT ($n= 2$) had a mean $d = 1.75$ ($SE = 0.52$) and a 95% confidence interval of 0.73 to 2.76, which was not significantly different from multidisciplinary CBT ($n= 2$) having a mean $d = 1.03$ ($SE = 0.43$) and a 95% confidence interval of 0.19 to 1.88; however, group CBT treatment ($n= 7$) was significantly different from both having a mean of $d = 0.49$ ($SE = 0.22$) and a 95% confidence interval of .06 to .93.

Table 3. *Variance components of the regression analysis by dependent variable*

Dependent Variable	Regression Variables			
	Attrition (R^2)	Number of Session (R^2)	Weeks (R^2)	Number of CBT Components (R^2)
Functional Status	.07	.30*	.01	.04
Pain	.001	.27*	.01	.01
Depression	.04	.21*	.02	.10
Anxiety	.02	.29*	.001	.07

Psychological Distress	.03	.38*	.36*	.19
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* $p \leq .05$

Table 4. *ANOVA comparisons for moderator's variables on the dependent variables*

	Moderator Variable	<i>n</i> (Effect sizes)	<i>Mean</i>	95% Confidence Interval
Treatment Modality				
Functional Status	Individual	3	0.74	-0.44 – 1.91
	Group	18	0.47	0.10 – 0.84
	Multidisciplinary	5	1.34	0.59 – 2.09
Pain	Individual	4	0.60	-0.35 – 1.56
	Group	25	0.67*	0.36 – 0.98
	Multidisciplinary	5	2.01*	1.27 – 2.74
Depression	Group	16	0.52*	0.23 – 0.81
	Multidisciplinary	4	1.46*	0.82 – 2.09
Anxiety	Group	23	0.44*	0.06 – 0.82
	Multidisciplinary	4	1.47*	0.74 – 2.20
Psychological	Individual	3	1.75*	0.73 – 2.76
	Group	9	0.49*	0.06 – 0.93
	Multidisciplinary	3	1.03*	0.19 – 1.88
Scientific Quality				
Functional Status	High	15	0.49	0.06 – 0.92
	Low	9	0.96	0.38 – 1.53
Pain	High	20	0.70	0.31 – 1.09
	Medium	4	0.56	-0.40 – 1.53
	Low	10	1.26	0.70 – 1.83
Depression	High	11	0.52	0.12 – 0.92
	Medium	3	0.41	-0.47 – 1.28
	Low	7	1.06	0.54 – 1.57
Anxiety	High	8	0.37	-0.15 – 0.88
	Medium	4	0.39	-0.40 – 1.18
	Low	6	1.23	0.62 – 1.84
Psychological	High	8	0.78	0.16 – 1.39
	Low	5	0.82	0.003 – 1.65

* $p \leq .05$, CBT = Cognitive Behavioral Therapy

DISCUSSION

This meta-analysis reviews the evidence in support of the use of CBT for individuals with fibromyalgia. Individuals with fibromyalgia experience many symptoms including pain, fatigue, decline in overall functioning, sleep problems, as well as, psychological sequelae such as depression, anxiety and general distress. This analysis found positive results for the application of CBT to individuals experiencing the symptoms of fibromyalgia. CBT can be helpful in reducing pain, depression, anxiety and general distress. Furthermore, CBT can be effective in increasing overall functioning in these individuals; this includes reduction in doctor's visits, improvements in physical functioning and overall improvements in quality of life.

Specifically, this meta-analysis found a moderate effect size for the improvement of functional status as a result of a CBT treatment. Functional status includes various constructs that are all related to the physical, social, and occupational functioning of a person as it relates to how they can manage their life and their pain. Furthermore, CBT for fibromyalgia was found to reduce pain symptoms in this study. The effect size was determined to be large, which was unexpected given that both reviews of CBT for fibromyalgia were skeptical of any effect CBT might have on pain (Bennett & Nelson, 2006; van Koulil et al., 2008). This review offers new evidence that CBT may reduce pain in people with fibromyalgia. However, these results must be interpreted cautiously as the 95% confidence interval was wide (see Table 5).

The psychological variables examined were found to have medium average effect sizes. In particular, the average effect size for depression was found to be medium. One hypothesis for this finding could be that CBT for individuals with fibromyalgia has an

effect on the somatic symptoms of depression, which may overlap with the experience of chronic widespread pain, but this would require further investigation. The average effect size for both anxiety and psychological distress were medium, confirming that CBT can be at least somewhat effective in reducing psychological distress and anxiety in individuals with fibromyalgia. All average effect sizes are summarized in the table below (see Table 5).

Table 5. *Average effect sizes across dependent variables*

Dependent Variable	Average Effect Size	95% Confidence Interval
Functional Status	0.65	0.30 – 0.99
Pain	0.85	0.53 – 1.17
Depression	0.69	0.34 – 1.04
Anxiety	0.66	0.22 – 1.10
Psychological Distress	0.76	0.37 – 1.14

Effect sizes should be considered in a larger scientific context, but for behavior sciences that one could use the general guidelines of “small”, medium” and “large” effect sizes as ≥ 0.20 , $= 0.50$, and ≥ 0.80 respectively (Cohen, 1977, 1988). This scientific community typically recognizes these guidelines to give meaning to effect size statistics. However, there is another way to examine the interpretation of effect sizes. More recently investigators have uses a “Fail-Safe N” to examine how many studies with an effect size of zero would be necessary to negate the results of the study (Rosenthal, 1979). This method attempts to counteract the “file-drawer problem” where studies with null effect sizes are not published, creating a bias. In this study, a conservative effect size

of 0.2 was selected because it would likely represent a non-significant effect size and would be considered “small.” For this meta-analysis 51 studies with an effect size of zero would be required to reduce the effect size of functional status to $d=0.20$. One hundred studies with an effect size of zero would be required to reduce the effect size of pain to $d=0.20$. Forty-four studies with an effect size of zero would be required to reduce the effect size of depression to $d=0.20$. Thirty-four studies with an effect size of zero would be required to reduce the effect size of anxiety to $d=0.20$. Thirty-three studies with an effect size of zero would be required to reduce the effect size of psychological distress to $d=0.20$. Thus, the results from this study appear to be robust.

The studies included in the analysis included a wide variety of study designs including randomized trials and pilot studies that did not include control group. This was done in an attempt to gather as much evidence as possible to determine the degree of various symptoms of fibromyalgia. Thus, all studies examining CBT in individuals with fibromyalgia were included regardless of scientific quality. A variable was created in an attempt to measure scientific quality. However, 60% of the studies were coded as high in scientific quality because they included a control group and the subjects were randomly assigned. Twelve percent of studies were coded as medium scientific quality, indicating that there was a control group, but groups were not randomly assigned. Thus, 28% of studies were coded in the “low” scientific quality, indicating that there were no comparison groups in the study. When ANOVAs were conducted to determine if there were significant differences in effect sizes between high, medium, and low scientific quality none of the analyses were significant (see Table 4). While mean effect sizes reported in Table 4 for scientific quality do appear to demonstrate a “trend” in that

studies coded as “low” in scientific quality have higher mean effect sizes in general, there was considerable variability in effect sizes across conditions.

Secondary analyses were performed on the data to determine if other aspects of the studies were contributing to the average effect sizes. Scientific quality of the studies, attrition rates, number of CBT components and number of weeks of treatment did not significantly contribute to the average effect sizes across dependent variables. However, the number of sessions indicated for treatment did account for a significant amount of the variance across average effect sizes across dependent variables. In particular, as the number of sessions increased the average effect sizes increased.

Furthermore, the type of CBT treatment, whether it be individual therapy, group therapy, or multidisciplinary therapy significantly impacted average effect sizes. In general, group therapy effect sizes were lower than both individual and multidisciplinary therapy. This may indicate that CBT group therapy for individuals may be less effective than individual treatment or multidisciplinary treatment. This is consistent with the results from the review of non-pharmacological treatments for fibromyalgia, which noted that CBT is typically more effective in combination than on its own (van Koulil et al., 2007). However, the majority of the studies included in the meta-analysis were measuring the effectiveness of group treatment (n=25), while a minority of studies included individual therapy (n=4) and multidisciplinary treatment (n=5).

In particular, one of the studies (Kroese et al., 2009) used a multidisciplinary therapy that contained eight upper bound outliers. In spite of this, the study was left in because it met all inclusion and exclusion criteria. All statistical analyses were run excluding this study. In this case, the average effect sizes across the dependent variables

were lower when the study was removed from the data. Furthermore, the ANOVA conducted to determine if types of CBT treatments contribute to the average effect sizes was non-significant across dependent variables when this study was removed. Thus, this study may have arbitrarily inflated effect sizes in the multidisciplinary group.

The results of this meta-analysis are not in direct conflict with conclusions drawn from recent literature reviews of CBT for fibromyalgia; however, the data presented above does serve to provide further evidence and clarification to reviews of the literature. Previous research has reviewed the use of psychological therapies for fibromyalgia. Beginning in 1999, Rossy et al. reviewed pharmacological and nonpharmacological therapies for fibromyalgia and determined that psychological therapies had medium positive effects for variables of physical status, self-report of fibromyalgia symptoms, psychological status and daily functioning (Rossy et al., 1999). In 2002, Sims and Adams conducted the first review of evidence for nonpharmacological therapies for fibromyalgia, at this point they determined that the available literature was inadequate to come to any conclusions about effectiveness of psychotherapy for individuals with fibromyalgia. At this point, they recommended that researchers use consistent measures for outcomes in their studies. Specifically they recommended the Fibromyalgia Impact Questionnaire (FIQ) in the current quantitative review, 16 out of 32 groups used the FIQ as an outcome measure (Burckhardt, Clark, & Bennett, 1991). Goldenberg (2004) conducted a systematic review of all therapies for fibromyalgia and suggests that low dose tri-cyclic antidepressants, exercise, CBT and patient education show preliminary effectiveness for the symptoms of fibromyalgia (Goldenberg, Burckhardt, & Crofford, 2004). In 2006, Bennett and Nelson specifically reviewed research using CBT as the

whole or part of the treatment for fibromyalgia. They determined that CBT can be effective making short term changes in pain-related behavior, coping strategies, and overall physical function; however, they questioned whether CBT could be effective in reducing pain in this population. Van Koulil et al. (2007) added that outcomes for non-pharmacological therapies are promising in the short term; however, outcomes may disappear long term. Two recent quantitative reviews (Glombiewski et al., 2010; Thieme & Gracely, 2009) have examined psychological interventions for fibromyalgia and found promising effect for pain reduction and in particular found improvement in functional status, depression, and catastrophizing. Furthermore, Glombiewski et al. (2010) found that psychological interventions can be effective over the long term.

In light of these findings, this study specifically examines the role of CBT in fibromyalgia, which appears to have the most evidence compared with other non-pharmacological interventions. Furthermore, the effect sizes found in this meta-analysis are somewhat higher than those reported in previous quantitative reviews (Glombiewski et al., 2010). The current study provides evidence in support of the effectiveness of CBT for symptoms of anxiety in individuals with fibromyalgia.

Limitations and future directions

The primary limitation of the evidence presented above is related to the inclusion criteria for this study. The analysis was completed on data from pre- and post- CBT intervention as opposed to a comparison of difference scores between control and treatment groups; thus, participants act as their own controls, not to a control group that did not receive treatment. The limitation of this method used in this study is that the effect sizes listed can only represent expected change of participant scores from before to

after treatment without controlling for other variables. This represents a fundamental difference from most meta-analyses performed in the field of chronic pain. Furthermore, it represents a difficulty in interpretation of the effect sizes obtained from this study, since prior meta-analyses in this field have not examined pre-post differences in their quantitative reviews, there is little with which to compare the results of this study.

Most studies were done with middle age women of unknown ethnicity and socioeconomic status. Attempts were made to document ethnicity and socioeconomic status for analysis; however, only a few of the studies documented these characteristics in their demographics. Thus, the demographics of the population to which these results apply are still unknown.

Internal validity of this study is in question due to the wide range of measures used to capture the dependent variables. This reduces confidence in the constructs themselves if they contain potentially different constructs within them. In meta-analysis, this represents the central controversy of apples vs. oranges. In particular, this meta-analysis used studies examining treatments which could all be classified as CBT, but which may include other treatment modalities such as medications or exercise in addition. This meta-analysis included a wide array of outcome measures that were assimilated into five distinct outcome measures. In an ideal world, researchers would have used consistent outcome measures to examine their dependent variables of interest. That said, many researchers have adopted common outcome measures such as the Fibromyalgia Impact Questionnaire (Burckhardt et al., 1991), as was recommended by (Sim & Adams, 2002). In this study, 16 of the 32 groups used the FIQ to measure outcomes. For example, it is possible to say that CBT for Fibromyalgia can reduce pain

symptoms, but we cannot say specifically that relaxation combined with cognitive restructuring will reduce Visual Analog Scale (VAS) pain scores.

While some attempt was made to measure scientific quality of these studies, by using a rating scale which differentiated between studies that were “high” (used a control group and assignment), “medium” (used a control group), “small” (did not have a control group), this effort was based on the assumption that utilized these designs would have been respectively rigorous in their implementation of other scientific controls. However, this assumption is questionable, and furthermore (as mentioned above), this meta-analysis did not examine the results of control groups, this study only examined the pre- and post outcomes of treatment groups. Therefore, the attempts made in this study to measure scientific quality are lacking in scientific quality.

Finally, it is not known how the effects of CBT change/remain over time. This study did not examine follow up data. While it was available for some of the studies in this meta-analysis, it was available for fewer than half of the studies and was not collected.

Improvements to this study to increase its scientific quality and relevancy would be to examine studies which provided follow up data to examine how effects change or remain the same over time. In a recent quantitative review, Glombiewski et al. (2010) reported that an increase in effect size was noted in studies that examined pain intensity over an average of 7.4 months; thus, long-term gains were maintained and even improved upon over time. Furthermore, the internal validity of this study could be improved by including only randomized control trials without other interventions included. For example, studies varied widely in their inclusion of medications in addition

to CBT in the treatment description, and some studies also included various forms of exercise. In order to truly examine the effect of CBT in individuals with fibromyalgia it would be necessary to only use studies that only examined CBT and compared it to a wait-list control, treatment as usual, or pharmacological approaches.

Additionally, one recommendation for future meta-analyses would be to include a standardized measure of scientific quality, such as the Jadad scale, typically used for randomized control trials (Jadad et al., 1996). Most scales rely heavily on whether treatments are blinded and how subjects are assigned to group; however, this would not be an effective way to capture scientific quality in this particular type of meta-analysis because they are based on the conditions applied to the control group and this meta-analysis only regards the treatment group. Rather, it would be important to capture other aspects such as sample characteristics (selection and homogeneity), attrition, threats to internal validity, and the reliability and validity of the outcome measures, which would likely capture scientific quality of the studies.

Conclusions/Summary

From the results of this meta-analysis, it can be summarized two moderators where found to impact effects sizes. The first, treatment duration was found to impact effect size, accounting for approximately one third of the variance in effect sizes notably across treatment outcomes. This finding has been replicated in other reviews of psychological treatments for fibromyalgia, which implies that individuals with fibromyalgia respond best to interventions with multiple sessions (Glombiewski et al., 2010; Thieme & Gracely, 2009; van Koulil et al., 2007). The other moderator that emerged from this analysis was that CBT that is situated within a multidisciplinary

program may be more effective than when provided individually or in a group setting. However, more evidence is necessary to confirm this finding because it is based on only five studies.

The field of psychological treatments for individuals with fibromyalgia has made significant gains in providing evidence for the effectiveness of these therapies, specifically CBT. Thirty-two groups were reviewed for this meta-analysis, which is a significant increase from the first review of this literature by Rossy et al. (1999), which examined evidence from 16 groups. However, considerable gaps still remain in the literature. First, researchers should continue to use commonly used, reliable and valid outcome measures for monitoring outcomes such as pain, functional status, depression, anxiety, fatigue and sleep problems. They should also continue to monitor outcomes over the long term and aim to develop interventions, which provide lasting effects. Furthermore, the research base would be strengthened by conducting more randomized blinded controlled studies to measure the effects of CBT and CBT in a multidisciplinary program, and research should be compared with exercise, and pharmacological therapies. Finally, related to recent research suggesting that different therapies may be more effective for certain individuals, it may be useful to examine treatment outcomes based on patient profiles such as those with adequate social support, those with significant emotional comorbidity, or those with high levels of pain.

In summary, while there are some limitations to this qualitative review, the evidence supporting the use of CBT to improve functioning, decrease pain, depression, anxiety and psychological distress is strong.

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APPENDIX A

Coding Manual

Study identification number (ID):

Bibliographic reference:

Publication year (YR):

Sample descriptors

Mean age: specify the approximate or exact mean age at the beginning of the intervention (if cannot be determined code: 999) (AGE)

Predominant sex of sample: exact proportion of women in the sample (SEX)

999 not reported

Average duration of fibromyalgia in the sample in years (DURATION) (if cannot be determined code: 999)

Is the sample taking medications? (MEDS)

1 Yes- not controlled

2 Yes- controlled/documented

3 No

99 Unable to determine

Research design descriptors

Type of therapy (UNIT)

1 Individual cbt

2 Group cbt

3 Multidisciplinary treatment

999 Cannot be determined

Scientific rigor (SCIR):

1 Random assignment + pre test differences (high)

2 Control group of any kind (medium)

3 No control group (low)

999 Cannot be determined

CBT Treatment group size (Start) (TXSIZE1) (999 Cannot tell)

CBT Treatment group size (End) (TXSIZE2) (999 Cannot tell)

Attrition (TXSIZE2/TXSIZE1x100)

Nature of the treatment descriptors

What are the components of CBT included in the treatment? (1=yes / 0=no)

Exposure, behavior mod (CBT_expbm)

Stress management (CBT_sm)

Problem solving (CBT_ps)

Relaxation training (CBT_rt)

Homework (CBT_hw)

Education (CBT_edu)

Support person involvement (CBT_sup)

Biofeedback (CBT_bio)

Self monitoring/goals (CBT_goal)

Cognitive restructuring (CBT_cr)
 Self-management of chronic pain (CBT_smcp)
 Exercise (CBT_ex)
 Sleep hygiene (CBT_sh)
 Assertiveness training/ social skills training (CBT_astss)
 Pleasant activity scheduling (CBT_pas)
 Relapse prevention (CBT_rp)

Duration of the treatment in weeks
 From pre test to post test (missing =999) (WEEKS)
 Number of treatment sessions (NO SESSION)
 Duration of sessions (minutes) (SESSDUR)
 Time to follow up in months (FUMONTHS1)
 Time to follow up in months (FUMONTHS2)
 Time to follow up in months (FUMONTHS3)
 Time to follow up in months (FUMONTHS4)

Effect size level coding manual

Effect size number (ESNUMBER)

Dependent measure descriptors:

Name of scale: (SCALNAME)

Type of scale: (SCALTYPE)

- 1 Self-report
- 2 Self-rated pain index - composite
- 3 Observers rating
- 4 Clinician ratings
- 5 Objective tests (physical)

Category of outcome construct/ specific measure: (CATOUT / CATSPEC)

1 Functional

- 1 Activity, MPI – activity
- 2 QWB
- 3 FIQ – physical
- 4 SF 36 – physical
- 5 SF 36 – functional, quality of life – EQ-D5
- 6 MPI – control/mastery (incl. csq)
- 7 FIQ – feeling good/wellbeing
- 8 Exercise (work capacity, functional capacity measurements, objective tests)
- 9 Visits to doctor
- 10 Functional disability – HAQ
- 11 VAS well being
- 12 IRGL disability

2 Pain

- 1 Intensity/severity (MPI/Q- Intensity and severity)
- 2 Self/Observer report of pain behaviors (OBS, Tubingen, PBCL, UAB)
- 3 VAS Pain score
- 4 Index/composite pain score
- 5 Myalgia score / Dolorimeter / Tender points

- 6 Interference (MPI)
- 7 FIQ – total
- 8 BPI
- 9 MPQ subscales (incl. - affective distress)
- 10 HAQ – symptoms soma/pain
- 11 FIQ – Pain
- 12 IRGL Pain
- 13 VAS Pain during exercise
- 3 Depression
 - 1 BDI
 - 2 VAS – Depression
 - 3 CES-D
 - 5 FIQ – feeling good
 - 6 FIQ – depression
 - 7 CDI
 - 11 IRGL Negative Mood
 - 12 SF36 MH composite score
- 4 Anxiety
 - 1 Fear (FS-III-R)
 - 2 MOCI – Obsessive Compulsive
 - 3 BAI
 - 4 FIQ – anxiety
 - 5 STAI – S/T
 - 6 PES – worry
 - 7 VAS – anxiety
 - 8 IRGL anxiety
- 5 psychosocial distress
 - 4 SCLR-90/BSI – GSI
 - 8 POMS
 - 9 MPI – affective
 - 10 PES/emotionality

Effect size data

Page number where the effect size was found (ESPAGE)

TX group size – total N at Posttest, i.e. useable data points (SSTX)

Treatment group mean pre-intervention (TX_PreMN)

Treatment group standard deviation pre-intervention (TX_PreSD)

Treatment group mean post-intervention (TX_PostMN)

Treatment group standard deviation post-intervention (TX_PostSD)

Effect size (ES)

Raw difference shows improvement (RAW)

- 1 Yes
- 2 No- Decline
- 3 No change (or statistically insignificant)
- 999 Cannot tell